

### REMARKS

Claims 1-6 are pending and rejected in the instant application. Claim 3 has been canceled without prejudice or disclaimer and claim 7 has been added. Claims 1, 2 and 4-7 are now under consideration in this case.

Claims 1, 2, 4-6 have been amended to incorporate a limitation from canceled claim 3; that is, the step of binding a specific substance to the array of porous polymer pads has been incorporated to distinctly claim the subject matter which the applicant regards as the invention. New Claim 7 recites a limitation from original claim 4; further support for this limitation can be found in the specification on page 5, line 7-8. In addition, the claims have been amended for clarity and for proper antecedent basis. No new matter has been added by way of these amendments.

Claims 1- 6 are rejected under 112, second paragraph as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention. Further, claims 1-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Guschin or Khrapko or Chetverin in view of Funk and if necessary, further in view of Ruchel (1978) or Ruchel (1975) or Blank.

Applicants respectfully traverse these rejections and provide remarks below in support of traversal. Hence, Applicants respectfully request that the above rejections to the pending claims be withdrawn.

Attached is an Appendix of Pending claims, entitled "**Version Of Claims Under Consideration With Markings To Show Changes Made**" which contains Claims 1, 2 and 4-7 under consideration and show the changes made by way of the amendments requested herein.

These amendments raise no new issues and the Applicants respectfully request that they be entered.

***Rejections Under 35 U.S.C. §112:***

Claim 1-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner has pointed out to the lack of proper antecedent basis in the claims and the lack of clarity in the recitation of steps in the method claim.

Applicants have amended the claims 1-2, 4-6 for clarity and proper antecedent basis, and have incorporated the Examiner's suggestions to overcome this rejection. Specifically, independent claims 1 and 5 have been amended to recite that the porous polymer pad is functionalized, and to incorporate a limitation from canceled claim 3 that, a specific substance is bound to each porous polymer pad, and that the gels are subsequently freeze-dried. Support for these amendments are found in the specification on page 5, line 7-9. Claims 2, 4 and 7 depend directly or indirectly on claim 1 and claim 6 on claim 5 and thus, incorporate all their limitations. Thus, Applicants respectfully request the withdrawal of the rejections to claims 1, 2, 4-6.

***Rejections Under 35 U.S.C. §103(a)***

Claims are rejected under 35 U.S.C. §103(a) as being unpatentable over Guschin or Khrapko or Chetverin in view of Funk and if necessary, further in view of Ruchel (1978) or Ruchel (1975) or Blank because the combination of the references discloses all the elements of the claims. Specifically, the Office action alleges that, since Funk discloses freeze-drying of a polymer gel to obtain a desired controlled pore size, and since Guschin, Khrapko and Chetverin disclose drying porous polymer gels, it would be obvious to freeze-dry the polymer gel of Guschin, Khrapko and Chetverin to obtain the controlled pore size as suggested by Funk. Applicants respectfully disagree with these allegations and traverse the rejection in view of the current claim amendments and since the Examiner has not provided a motivation to combine.

Guschin and Khrapko do not teach freeze-drying gels. Guschin teaches microchips with 3-dimensional gel pads for a greater binding capacity for oligonucleotide probes than 2-dimensional glass supports. Guschin teaches drying and storage of these microchips for future reuse. However, Guschin does not teach drying to increase the pore size of the gel; rather, Guschin dries the gels for storage.

Khrapko teaches oligonucleotide gel arrays and a plurality of mechanically spaced dots to localize oligonucleotides within a selected gel volume. As the Examiner admits, Khrapko does not teach or suggest freeze-drying gels to increase the pore size of the gel.

Chetverin et al. provides a method for the amplification of nucleic acids entrapped in a porous, gel matrix. This reference teaches drying gels by lyophilization before soaking with

enzymes. However, the nucleic acids are not bound to the gel as required by the present claims. Additionally, Chetverin does not teach an array.

Funk et al. provides a process for the preparation of porous, hydrophilic, highly swellable hydrogels using freeze-drying techniques and teaches achieving "desired pore size." But Funk does not teach or suggest the use of such porous hydrogels in binding assays for specific substances such as polynucleotides.

Blank et al. and Ruchel (1975) teach freeze-drying of polyacrylamide gels and provide scanning electron micrographs of the dehydrated gel to show its sponge-like structure. Ruchel (1978) teach freeze-etching a slab gel during Transmission Electron Microscopy (TEM). None of these references teach or suggest freeze-drying gels for binding assays, particularly with binding substances attached.

In contrast, the claimed invention is directed to an improvement of an array of porous polymer pads with bound substances like polynucleotides by freeze-drying gels to increase pore size so that large target molecules can easily diffuse into the gels in binding assays. Here, the gel is freeze-dried after the substance, e.g., DNA, is bound to the gel. Increased pore size increases the signal-to-noise ratio compared to conventional gel pads (see p. 13).

As the Examiner is aware, the test for obviousness is whether the claimed invention as a whole would have been obvious at the time it was made to a person of ordinary skill in the art. A *prima facie* case of obviousness requires that (1) there must be some suggestion or motivation, either in the references or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; and (2) there should be a reasonable

expectation of success; See M.P.E.P. § 2142. If any one of these criteria is not met, a *prima facie* case of obviousness is not established.

As a preliminary matter, the Applicant submit that Funk is non-analogous art. "In order to rely on a reference as a basis for rejection of an Applicant's invention, the reference must either be in the field of the applicants's endeavour, or, if not, then be reasonably pertinent to the particular problem with which the inventor was concerned". *In re Oetiker*, 977 F.2d 1443, 1446, 24 USPQ2d 1443, 1445 (Fed. Cir. 1992); MPEP Section 2141.01 (a).

Funk uses porous, swellable hydrogels in products such as diapers, sanitary towels and other hygiene products and as water-retentive agents in agricultural horticulture (see column 1, lines 17-20). Funk does not teach or suggest the use of freeze-dried gels in gel arrays used in binding assays and hence Applicants submit that Funk's hydrogels are not in the field of the Applicant's endeavor. Accordingly, Funk cannot provide motivation to one of skill in the art to combine it with Guschin, Khrapko and Chetverin unless these references desire such a combination.

The Examiner's reasons for combining Guschin, Khrapko and Chetverin with Funk is because "it would be expected that freeze-drying increases the pore size". The Examiner has not clearly cited motivation in these references. Applicants once again respectfully remind the Examiner that "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." *In re Mills*, 16 USPQ2d 1430 (Fed. Cir. 1990); M.P.E.P. § 2143.01. Also, the law states that, "the teaching or suggestion to make the claimed invention, as well as the

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reasonable expectation of success must come from the prior art, not the Applicant's disclosure" *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP Section 706.02(j). Applicants also add that the Examiner has not provided motivation to combine the Guschin, Khrapko and Chetverin with Blank, Ruchel (1978) or Ruchel (1975) nor do these references desire such a combination. Absent evidence of explicit or implicit motivation to combine references, Applicants submit that the Examiner has failed to establish a *prima facie* case of obviousness.

In view of the above remarks, Applicants submit that a *prima facie* case of obviousness has not been established. Thus, Applicants respectfully request withdrawal of the rejection of claims under 35 U.S.C 103(a).

### CONCLUSION

Applicants respectfully submit that claims are now in condition for allowance and an early notification of such is requested.

The Examiner is invited to call the undersigned attorney for discussion of any outstanding issues.

Respectfully submitted,

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Filed under 37 C.F.R. § 1.34(a)

Dated: \_\_\_\_\_

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APPENDIX

"Version Of Claims Under Consideration With Markings To Show Changes Made"

1. (Twice Amended) ~~In A method of providing~~ <sup>providing</sup> ~~improving~~ an array of porous polymer pads ~~used in binding assays, on a solid support and then drying the array of porous polymer pads on said solid support, the said improvement carrying out said drying by freeze drying by a method comprising:~~  
a. providing said array of porous polymer pads on the surface of a solid support, wherein said porous polymer pads are functionalized;  
b. binding a specific substance to each porous polymer pads;  
c. freezing said array of porous polymer pads on said solid support; and,  
d. drying said array of porous polymer pads on said solid support at reduced pressure;  
wherein, said freeze-drying increases the pore size of ~~the~~ said porous polymer pads.
2. (Twice Amended) An array of freeze-dried porous polymer pads on a solid support, comprising a specific substance bound to each of the porous polymer pads, prepared using the steps of claim 1.  
~~wherein said porous polymer pads are freeze dried by:~~  
a. ~~providing an array of porous polymer pads on a solid support,~~  
b. ~~freezing said array on said solid support, and~~  
c. ~~drying said array on said solid support at reduced pressure,~~  
~~thereby increasing pore size in the said porous polymer.~~
3. CANCELED.
4. (Amended) The array of claim 3 2 wherein the said specific ~~binding~~ substance is a probe polynucleotide.
5. (Amended) A method ~~for freeze drying an array comprising~~ for increasing the pore size of the porous polymer pads on a solid support in an array used in binding assays, said method comprising:  
a. providing said array of porous polymer pads on the surface of a solid support;  
b. binding a specific substance to said array of porous polymer pads;  
c. freezing said array of porous polymer pads on said surface; ~~on said solid support;~~ and,  
d. drying said array of porous polymer pads on said surface ~~on said solid support~~ at reduced pressure.

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6. (Amended) The method of claim 5 wherein ~~the~~ said freezing is porous polymer pads are ~~frozen~~ at liquid nitrogen temperatures and said drying is ~~dried under vacuum to remove~~ water by sublimation.
7. (New) The array of claim 4 wherein said probe is a polynucleotide.